



BOSTON, MASSACHUSETTS 02109-1784
TELEPHONE (617) 227-7400
FAX (617) 742-4214
www.lahiye.com

JOHN A. LAHIVE, JR. (1928-1997) JAMES E. COCKFIELD (1930-2005) THOMAS V. SMURZYNSKI GIULIO A DeCONTI JR ELIZABETH A. HANLEY AMY BAKER MANDRAGOURAS ANTHONY A. LAURENTANO KEVIN J. CANNING JANE E. REMILLARD DEBRA J. MILASINCIC, Ph.D. MEGAN E. WILLIAMS, Ph.D. WILLIAM A. SCOFIELD, JR. SIBLEY P. REPPERT DAVID R. BURNS JOHN S. CURRAN SEAN D. DETWEILER HATHAWAY P. RUSSELL * MARIA LACCOTRIPE ZACHARAKIS, Ph.D. DANIELLE L. HERRITT

EUIHOON LEE **
MANEESH GULATI
CYNTHIA M. SOROOS
PETER W. DINI, Ph.D.
MICHAEL J. BASTIAN, Ph.D.
CHRISTOPHER J. MCKENNA
VINCENT P. LOCCISANO
JAMES M. MCKENZIE
LEIGH J. MARTINSON
JILL R. GORNY
SAPNA MEHTANI, Ph.D.

OF COUNSEL
JEREMIAH LYNCH
JEANNE M. DIGIORGIÓ
CYNTHIA L. KANIK, Ph.D.
BENEDICT A. MONACHINO

PATENT AGENTS
CRISTIN E. HOWLEY, Ph.D.
JILL ANN MELLO, Ph.D.
CHRISTOPHER E. DRABIK
JAMES H. VELEMA
JACOB G. WEINTRAUB
BRIAN C. TRINQUE. Ph.D.

TECHNICAL SPECIALISTS
CATHERINE M. BISHOP
DEBORAH L. NAGLE, Ph.D.
ANNE JACQUELINE WIZEMAN, Ph.D.
CHRISTOPHER R. COWLES, Ph.D.
W. ELANA WANG
MEAGHAN L. RICHMOND, Ph.D.
SHARON M. WALKER, Ph.D.
LAURA C. DILORENZO
ALISSA H. ENCK

- * Admitted in TX only
- ** Admitted in CT only

September 14, 2005

MS Amendment Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450

Re:

U.S. Patent Application No.: 10/700,816

For: ALLELE-SPECIFIC RNA INTERFERENCE

Inventors: Zuoshang Xu, et al. Filed: November 4, 2003 Our Ref. No.: UMY-038

Dear Sirs:

I enclose herewith for filing in the above-identified application the following:

- 1. Information Disclosure Statement;
- 2. PTO Form SB/08;
- 3. A copy of the International Search Report;
- 4. Copies of selected references cited in PTO Form SB/08 (28); and
- 5. A Return Postcard.

No additional costs are believed to be due in connection with the filing of this Information Disclosure Statement. However, please charge any necessary fees in connection with the enclosed statement to our Deposit Order Account No. 12-0080. For this purpose, a duplicate of this sheet is attached.

I hereby certify that this correspondence is deposited with the United States Postal Service as first class mail in an envelope addressed to:

MS Amendment, Commissioner for Patents, P.O. Box 1450,
Alexandria, Virginia 22813-1450 on:

/ Mate / / /

Debra J. Milasincic, Reg. No. 46, 931

Respectfully submitted

LAHIVE\& COCKFIELD, LLP

Debra J. Milasincic Registration No. 46, 931 Attorney for Applicants



THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Zuoshang Xu, et al.

Serial No.: 10/700,816

Filed: November 4, 2003

For: ALLELE-SPECIFIC RNA INTERFERENCE

Attorney Docket No.: UMY-038

MS Amendment

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Certificate of First Class Mailing (37 CFR §1.8(a))

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: MS Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313/1450 on the date set forth below.

<u>September 14, 2005</u>

Date of Signature and of Mail Deposit

Debra J. Milasincic, Esq.

Group Art Unit: 1632

Examiner: Not Yet Assigned

Reg. No. 46,931

Attorney for Applicants

INFORMATION DISCLOSURE STATEMENT

Dear Sir:

Applicants and their Attorney are aware of the following publications and information, listed on the attached PTO Form SB/08, and in accordance with 37 CFR §1.97 hereby submit these publications for the Examiner's consideration. Reference ID Nos. A1 and C4 were cited in an International Search Report dated May 27, 2004 during the prosecution of PCT/US03/35009 which corresponds to the above referenced application. A copy of the report and each cited publication is enclosed.

This statement is not to be interpreted as a representation that the cited publications are material, that an exhaustive search has been conducted, or that no other relevant information exists. Nor shall the citation of any publication herein be construed *per se* as a representation that such publication is prior art. Moreover, the Applicants understand that the Examiner will make an independent evaluation of the cited publications.

Under 37 CFR § 1.97(b)(3), no additional costs are believed to be due in connection with the filing of this disclosure. If, however, a first Office Action on the merits issues in this application bearing a mailing date prior to the date of this Information Disclosure Statement, please charge the appropriate fee as required under 37 CFR §1.17(p) to our Deposit Order Account No. 12-0080.

Respectfully submitted, LAHIVE & COCKFIELD, LLP

Debra J. Milasincic, Esq. Registration No. 46,931 Attorney for Applicants

28 State Street Boston, MA 02109 (617) 227-7400

Date: September 14, 2005

DJM/JHV Enclosures

SEP 1 6 2005 THAT & IBADEN

PTO/SB/08a/b (08-03)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Sub	stitute for form 1449A/B/F	PTO		Complete if Known		
				Application Number	10/700,816	
١N	IFORMATIO	N DI	SCLOSURE	Filing Date	November 4, 2003	
S	TATEMENT	BY A	APPLICANT	First Named Inventor	Zuoshang Xu	
				Art Unit	1632	
	(Use as many s	sheets as	necessary)	Examiner Name	Not Yet Assigned	
Sheet	1	of	3	Attorney Docket Number	UMY-038	

			U.S. PA	TENT DOCUMENTS	
Examiner Initials*	Cite No.1	Document Number Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	2003/0180756 A1	09-25-2003	Shi, Y., et al.	
	A2	2003/0190635 A1	10-09-2003	McSwiggen, J.A.	
	A3	2004/0192629 A1	09-30-2004	Xu, Z., et al.	
	A4	2004/0214198 A1	10-28-2004	Rana, T.M	
	A5	2004/0219671 A1	11-04-2004	McSwiggen, J.A., et al.	
	A6	2004/0241854 A1	12-02-2004	Davidson, B.L., et al.	
	A7	2004/0023390 A1	02-05-2004	Davidson, B.L., et al.	•
	A8	2005/0042646 A1	02-24-2005	Davidson, B.L., et al.	
	A9	2005/0130184 A1	06-16-2005	Xu, Z., et al.	
	A10	2005/0130919 A1	06-16-2005	Xu, Z., et al.	
	A11	2005/0137155 A1	06-23-2005	McSwiggen, J.A., et al.	

		FOREI	GN PATENT	DOCUMENTS		
Examiner Initials*	Cite No.1	Foreign Patent Document Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
	В1	WO 03/070895 A2	08-28-2003	Ribozyme Pharmaceuticals, Inc.		
	B2	WO 03/080807 A2	10-02-2003	President and Fellows of Harvard College		
	ВЗ	WO 2004/013280 A2	02-12-2004	University of lowa Research Foundation		
	B4	WO 2004/01335 A1	02-12-2004	University of Iowa Research Foundation		
	B5	WO 2004/013310 A2	02-12-2004	Intradigm Corporation		
	В6	WO 2004/042027 A2	05-21-2004	University of Massachusetts		-
	В7	WO 2004/046324 A2	06-03-2004	University of Massachusetts		
	В8	WO 2004/058940 A2	07-15-2004	University of Iowa Research Foundation		
	В9	WO 2005/003350 A2	01-13-2005	Ribozyme Pharmaceuticals, Inc.		
	B10	WO 2005/007875 A2	01-27-2005	University of Massachusetts		
	B11	WO 2005/007877 A2	01-27-2005	University of Massachusetts		Γ
	B12	WO 2005/023991 A2	03-17-2005	The General Hospital Corporation		
	B13	WO 2005/027980 A1	03-31-2005	University of Massachusetts		

Examiner	Date	i
Signature	Considered	

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Sut	ostitute for form 1449A/B/PT	0		Complete if Known		
		•		Application Number	10/700,816	
11	NFORMATION	l DI	SCLOSURE	Filing Date	November 4, 2003	
l s	TATEMENT B	3Y /	APPLICANT	First Named Inventor	Zuoshang Xu	
				Art Unit	1632	
	(Use as many sh	eets as	s necessary)	Examiner Name	Not Yet Assigned	
Sheet	2	of	3	Attorney Docket Number	UMY-038	

	FOREIGN PATENT DOCUMENTS								
Examiner Initials*	Cite No.1	Foreign Patent Document Country Code ³ -Number ⁴ -Kind Code ⁵ (<i>if known</i>)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶			
	B14	WO 2005/045034 A2		Ribozyme Pharmaceuticals, Inc.					

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁸ Applicant is to place a check mark here if English language Translation is attached.

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
	C1	Harper, S.Q., et al. "RNA interference improves motor and neuropathological abnormalities in a Huntington's disease mouse model." Proc Natl Acad Sci USA. 2005 Apr 19; 102(16): 5820-25	
	C2	Maxwell, M.M., et al. RNA interference-mediated silencing of mutant superoxide dismutase rescues cyclosporin A-induced death in cultured neuroblastoma cells." Proc Natl Acad Sci USA 2004 Mar. 2; 101(9): 3178-83	
	СЗ	Miller, V.M., et al. "Targeting Alzheimer's desease genes with RNA interference: an efficient sttrategy for silencing mutant alleles." Nucleic Acids Research Oxford University Press 2004; 32(2): 661-668	
	C4	Ralph, S.G., et al. "Silencing mutant SOD1 using RNAi protects against neurodegeneration and extends survival in an ALS model" Nature Medicine. 2005 Apr; 11(4)	
	C5	Raoul, C. et al. "Lentiviral-mediated silencing of SOD1 through RNA interference retards disease onset and progression in a mouse model of ALS." Nature Medicine. 2005 Apr; 11(4)	
	C6	Rival, T. et al. "Decreasing glutamate buffering capacity triggers oxidative stress and neuropil degeneration in the <i>drosophila</i> brain." <i>Current Biology</i> . 2004 Apr. 6; 14:599-605.	
	C7	Sui G., et al. "A DNA vector-based RNAi technology to suppress gene expression in mammalian cells." Proc Natl Acad Sci USA 2002 Apr 16;99(8): 5515-5520	
	C8	Veldink, J.H., et al. "The future of motor neuron disease." J Neurol. 2004; 251:491-500.	
	C9	Xia, X.G., et al. "An enhanced U6 promoter for synthesis of short hairpin RNA." Nucleic Acids Res. 2003 Sep 1; 31(17):e100 (5 pages).	
	C10	Xia, X.G., et al. "An RNAi strategy for treatment of amyotrophic lateral sclerosis caused by mutant Cu,Zn superoxide dismutase." J Neurochem. 2005 Jan; 92(2):362-7	
	C11	Xie, J., et al. "RNAi knockdown of Par-4 inhibits neurosynaptic degeneration in ALS-linked mice." J Neurochem. 2005 Jan; 92(1):59-71.	
	C12	Xie, Z., et al. "Effects of RNA interference-mediated silencing of γ-secretase complex components on cell sensitivity to caspase-3 activation." The Journal of Biological Chemistry. 2004 Aug 13; 279(33):34130-7.	

Examiner	Date
Signature	Considered

PTO/SB/08a/b (08-03)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Su	bstitute for form 1449A/E	R/PTO		Complete if Known		
"	ballate for form 1440/01	<i>3</i> /1 1 0		Application Number	10/700,816	
	NFORMATION	ON DISC	CLOSURE	Filing Date	November 4, 2003	
5	TATEMEN	T BY AF	PPLICANT	First Named Inventor	Zuoshang Xu	
				Art Unit	1632	
	(Use as many	sheets as ne	ecessary)	Examiner Name	Not Yet Assigned	
Sheet	3	of	3	Attorney Docket Number	UMY-038	

	NON PATENT LITERATURE DOCUMENTS	
Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
C13	Miller, V.M., et al. "Allele-specific silencing of dominant desease genes." Proc Natl Acad Sci USA. 2003 Jun 10; 100(12): 7195-7200	
C14	Ding, H. et al., "Selective silencing by RNAi of a dominant allele that causes amyotrophic lateral sclerosis" Aging Cell 2003;2:209-217	
	No. ¹ C13	Cite Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. C13 Miller, V.M., et al. "Allele-specific silencing of dominant desease genes." Proc Natl Acad Sci USA. 2003 Jun 10; 100(12): 7195-7200 C14 Ding, H. et al., "Selective silencing by RNAi of a dominant allele that causes amyotrophic

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Examiner	 Date	
Signature	Considered	

¹Applicant's unique citation designation number (optional). ²Applicant is to place a check mark here if English language Translation is attached.